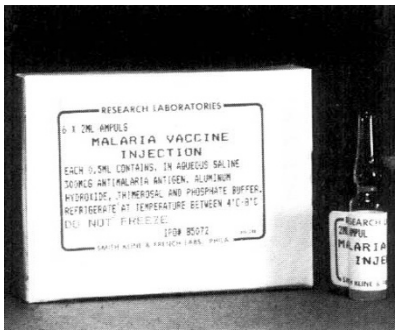
MEETING REPORT

CLONED MALARIA VACCINE ENTERS THE CLINIC

WASHINGTON, D.C.—On March 17, human trials of the first antimalarial vaccine began.

Based on a cloned repeated sequence derived from the circumsporozoite gene of the malaria parasite *Plasmodium falciparum*, and expressed in *Escherichia coli* (see *Bio/Technology* 3:519, June '85), the vaccine results from collaborative efforts between scientists at Smith Kline & French (Philadelphia, PA) and the Walter Reed Army Institute of Research (Washington, D.C.). According to J. D. Chulay (Walter Reed), who described the design of the phase I and II trials at an American Society for Microbiology symposium here, this is the "purest vaccine ever administered to humans," containing less than 20 nanograms of nucleic acid, and less than 5 units of endotoxin, per milligram of protein.

The phase I trials now underway are designed to determine safety and immunogenicity. Initially, volunteers in five groups are being given three injections each—in doses ranging between 10 and 800 micrograms of protein—at four week intervals. If sera from any of the groups prevents invasion of cultured human liver cells by sporozoites, or has a high circumsporozoite precipitin titer, phase II challenges will be initiated.



Ampules of FSV-1 (Falciparum Sporozoite Vaccine-1) containing recombinant circumsporozoite antigen formulated with aluminum hydroxide. The vaccine is currently undergoing phase I clinical trials at the Walter Reed Army Hospital.

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An often-voiced potential problem with a sporozoite vaccine is that infecting parasites are quickly sequestered in the liver, and thus if even one escaped neutralization by circulating antibodies, breakthrough infection would occur. But two sets of experiments reported at the symposium suggest this might not be the case

Wayne Hockmeyer (Walter Reed, discussed work done in collaboration with Dominique Mazur at the University of Paris. They treated cultured human liver cells with suboptimal concentrations of antibodies induced by the vaccine construct, infected the culture, and followed the development of intracellular parasites. Surprisingly, even after six days, the cells remained free of any viable intrahepatocyte forms.

Equally encouraging was the report by Ruth Nussenzweig (New York University) that gamma interferon completely inhibited the development of liver forms of the rodent malaria parasite, and appreciably delayed the onset of parasitemia in chimpanzees. Nussenzweig suggested that immunization with an antisporozoite vaccine would prime T cells to release gamma interferon after infection, and in this way liver cells might be protected from any parasites that escaped the effects of the immune sera.

—Harvey Bialy